

IT IS CLAIMED:

1. A method of reducing the risk of restenosis in a region of a patient's coronary vessel which has been treated by coronary angioplasty using a catheter with a distal-end expandable balloon, or which is at a junction formed in a coronary bypass operation, said method comprising

administering to the patient, by local administration directly to the vessel site of injury, a morpholino antisense compound having (i) from 8 to 40 nucleotides, including a targeting base sequence that is complementary to a region that spans the start codon of a human *c-myc* mRNA gene, and (ii) uncharged, phosphorous-containing intersubunit linkages, in an amount effective to reduce the risk of restenosis in the patient, where said administering is carried out by a mode of administration selected from the group consisting of

(a) contacting the region of the vessel with a reservoir containing the antisense compound, and introducing the compound from the reservoir into the vessel by iontophoresis or electroporation;

(b) injecting the compound from the catheter directly into the region of the vessel, under pressure, through injectors contained on the surface of the catheter balloon, where said injectors are capable of penetrating the tunica media in the vessel;

(c) injecting into or contacting the region of the vessel, microparticles containing the antisense compound in entrapped form;

(d) contacting the region of the vessel with a hydrogel coating contained on the surface of the catheter balloon, and containing the antisense compound in diffusable form; and

(e) contacting the region of the vessel with a stent having an outer surface layer containing the antisense compound in diffusable form.

2. The method of claim 1, wherein the intersubunit linkages are selected from the group consisting of the structures presented in Figs. 2AA-2EE.

3. The compound of claim 2, wherein the linkage is the phosphorodiamidate linkage represented at Figure 2B-B, where $X = NH_2$, $Y = O$, and $Z = O$.

4. The method of claim 3, wherein the antisense compound has the sequence identified by SEQ ID NO:1.

5. The method of claim 1, wherein the amount of antisense compound administered is between about 0.5 and 20 mg.

6. The method of claim 1, for use in mode of administration (a), wherein the antisense compound is contained in a volume between two inflated balloons in the catheter, the compound contains a net charge, and the volume is subjected to pulsed electric fields effective to iontophoretically drive the compound into region of the vessel.

7. The method of claim 1, for use in mode of administration (a), wherein the antisense compound is contained in a volume between two inflated balloons in the catheter, and the volume is subjected to pulsed electric fields effective to facilitate compound uptake into vessel-region cells by electroporation.

8. The method of claim 1, for use in mode of administration (b), wherein the catheter balloon has a plurality of outer-facing channels that communicate with a distal-tip reservoir, each channel having one or more injection ports, and said injecting includes forcing a solution or suspension of the antisense compound from said reservoir through said injection ports when the balloon is in an inflated position.

9. The method of claim 1, for use in mode of administration (c), wherein the catheter has a distal end reservoir, the microparticles are contained as a particle suspension in the reservoir, and said injecting includes forcing the suspension out of the catheter through a catheter surface in contact with the vessel region.

10. The method of claim 9, wherein the particles are microbubbles containing the antisense compound in entrapped form, and the method further includes exposing the vessel region to ultrasonic energy following the particle injection.

11. The method of claim 1, for use in mode of administration (d), wherein the coating is designed to release the majority of the antisense compound in the coating over a period of 5-60 minutes following balloon angioplasty.

12. The method of claim 1, for use in mode of administration (e), wherein the stent is biodegradable, and is designed to release the majority of the antisense compound in the coating over a period of 5-60 minutes following balloon angioplasty.

13. A method of treating the risk of restenosis in a region of a patient's coronary vessel, comprising

administering to the patient, by local delivery directly into the region of injury, a morpholino antisense compound having (i) the base sequence identified as SEQ ID NO:1, and (ii) a phosphorodiamidate backbone shown in Figure 2B-B, where $X = NH_2$, $Y = O$, and $Z = O$, where said administering is by placing the compound in direct contact with the vessel region, in an amount effect to deliver between about 0.5 to 2 mg antisense compound to the tissue-vessel region.

14. The method of claim 13, wherein the compound is derivatized with a moiety that enhances the solubility of the compound in aqueous medium, and the compound is administered from a solution containing at least about 30 mg/ml of the antisense compound.

15. The method of claim 14, wherein said moiety is triethyleneglycol attached to the 5' end of the compound.

16. A morpholino antisense compound having (i) from 8 to 40 nucleotides, including a targeting nucleic acid sequence complementary to a region that spans the start codon of a human *c-myc* mRNA gene, and (ii) uncharged, phosphorous-containing intersubunit linkages.

17. The compound of claim 16, wherein the intersubunit linkages are selected from the group consisting of the structures presented in Figs. 2A-A-2E-E.

18. The compound of claim 17, wherein the linkage is the phosphorodiamidate linkage represented at Figure 2B-B, where X=NH₂, Y=O, and Z=O.

19. The compound of claim 16, wherein the antisense compound has the sequence identified by SEQ ID NO: 1.

20. The compound of claim 19, wherein the compound is derivatized with a moiety that enhances the solubility of the compound in aqueous medium, to a level of at least about 30 mg/ml of the antisense compound.

21. The compound of claim 20, wherein said moiety is triethyleneglycol attached to the 5' end of the compound.

22. The compound of claim 16, which is entrapped in liposomal or biodegradable microparticles.

23. In a method aimed at reducing the risk of restenosis in a region of a patient's coronary vessel which has been treated by coronary angioplasty using a catheter with a distal-end expandable balloon, by administering to the vessel region, an antisense compound directed against a target human *c-myc* mRNA sequence, a method for assaying the ability of the antisense compound to reach and interact with *c-myc* mRNA in vessel cells, comprising

administering to the patient, a morpholino antisense compound having a substantially uncharged backbone, and a sequence that spans the start codon of the human *c-myc* gene,

at a selected time after said administering, taking a sample of a body fluid from the subject, and

detecting in said sample the presence of a nuclease-resistant heteroduplex composed of the antisense compound and the target RNA region.

24. The method of claim 23 wherein the body-fluid is urine.

25. The method of claim 23, wherein said detecting is accomplished by reacting the sample with an antibody specific against said heteroduplex, and detecting the presence of the antibody-heteroduplex conjugate.